Complete Summary

GUIDELINE TITLE

Neurologic complications.

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Neurologic complications. New York (NY): New York State Department of Health; 2004 Mar. 26 p. [31 references]

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

- June 15, 2005, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): U.S. Food and Drug Administration (FDA) recommended proposed labeling for both the prescription and over the counter (OTC) NSAIDs and a medication guide for the entire class of prescription products.
- April 7, 2005, Non-steroidal anti-inflammatory drugs (NSAIDS) (prescription and OTC, including ibuprofen and naproxen): FDA asked manufacturers of prescription and non-prescription (OTC) non-steroidal anti-inflammatory drugs (NSAIDs) to revise their labeling to include more specific information about potential gastrointestinal (GI) and cardiovascular (CV) risks.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Human immunodeficiency virus (HIV) infection
- HIV-associated neurologic complications:
    - HIV-associated dementia
    - HIV-associated myelopathy
    - Peripheral neuropathy
    - Myopathy
    - HIV-associated neuromuscular weakness syndrome

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Neurology
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To help medical providers correctly diagnose and properly manage the symptoms and signs of neurologic complications that may be found in HIV-infected patients

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients with neurologic complications

INTERVENTIONS AND PRACTICES CONSIDERED

Management of HIV-Associated Dementia (HAD)

1. Neurologic examination using standardized tools and careful substance use history
2. Laboratory tests including vitamin B_{12} and folate, serum syphilis screen (rapid plasma reagin [RPR] or venereal disease research laboratory [VDRL] test), serum cryptococcal antigen, thyroid function tests, cerebrospinal fluid (CSF) testing if indicated
3. Neuroimaging studies (magnetic resonance imaging [MRI], computed tomography [CT])
4. Referral to a neuropsychologist or psychiatrist
5. Antiretroviral (ARV) therapy and pharmacologic treatment of symptoms (e.g., psychotropic medication)

Management of HIV-Associated Myelopathy

1. Neurological examination
2. Laboratory tests including serum RPR or VDRL, toxoplasma antibodies, cryptococcal antigen, vitamin B_{12} level, human T-lymphocyte virus I/II antibodies, and CSF studies
3. Spine MRI
4. Electrophysiologic studies (e.g., somatosensory evoked potentials)
5. Symptomatic therapy for myelopathy

Management of Peripheral Neuropathy

1. Neurological examination
2. Blood tests and lumbar puncture
3. Electrophysiologic studies such as electromyography (EMG), nerve conduction velocity (NCV)
4. Nerve biopsy
5. MRI (to diagnose progressive polyradiculopathy)
6. Referral to a neurologist
7. Pain control including acetaminophen, aspirin, or non-steroidal anti-inflammatory drugs with or without adjuvant agents such as anticonvulsants, antidepressants or topical agents; narcotic analgesia
8. ARV dose reduction or substitution of a less neurotoxic ARV
9. Immunomodulating therapy including corticosteroids, high-dose intravenous immunoglobulin, plasmapheresis
10. ARV discontinuation in cases of hyperlactatemia or lactic acidosis
11. Anti-cytomegalovirus (CMV) therapy
12. Initiation or optimizing highly active antiretroviral therapy (HAART)

Management of Myopathy

1. Neurological examination
2. Serum creatine phosphokinase (CPK) levels
3. EMG and muscle biopsy
4. Referral to a neurologist or rheumatologist
5. Corticosteroids, intravenous immunoglobulin

Management of HIV-Associated Neuromuscular Weakness Syndrome

1. Complete neurologic examination

2. Blood tests including serum lactate level, serum bicarbonate and arterial pH, serum CPK
3. Electromyography–nerve conduction velocities (EMG–NCV)
4. Nerve and muscle biopsy
5. Consultation with a neurologist
6. Discontinuing the use of nucleoside reverse transcriptase inhibitors (NRTIs)
7. Initiating treatment for lactic acidosis and supportive treatment for muscle weakness

MAJOR OUTCOMES CONSIDERED

- Utility of diagnostic tests
- Effectiveness of treatment in terms of viral suppression and pain control

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Committee
- Women's Health Committee
- Substance Use Committee
- Physician's Prevention Advisory Committee
- Pharmacy Committee

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence (I-III) is defined at the end of the "Major Recommendations" field.

Human Immunodeficiency Virus (HIV)-Associated Dementia (HAD)

When patients with HAD present with accompanying depression, mania, psychosis, behavioral disturbance, or substance use, primary care clinicians should refer for psychiatric consultation to assist in psychopharmacologic treatment and management. (**I**)

Clinicians should use standardized tools to stage HAD. (**III**)

Key Point:

Psychiatric consultation may assist in differentiating between HAD and pseudodementia, and between HAD and cognitive impairment due to mania, psychosis, delirium, substance use, or psychotropic or HIV-related medications. Neuropsychological testing may also be helpful with diagnostic assessment.

Key Point:

The early signs and symptoms of HAD are often subtle and difficult to recognize.

Refer to Table 1 in the original guideline document for information on clinical manifestations of HIV-associated dementia.

Diagnosis

The following tests should be performed to exclude other possible etiologies of cognitive dysfunction: (**III**)

- Vitamin B_{12} and folate levels
- Serum syphilis screen (rapid plasma reagin [RPR] or venereal disease research laboratory [VDRL] test)
- Serum cryptococcal antigen
- Thyroid function tests

Cerebrospinal fluid testing to exclude other central nervous system infections that may cause cognitive dysfunction, such as neurosyphilis, cytomegalovirus encephalitis, tuberculous meningitis, and cryptococcal meningitis, should be performed when clinically indicated. (**I**)

Clinicians should obtain neuroimaging in patients with cognitive dysfunction. (**I**)

Clinicians should refer patients to a neuropsychologist for detailed neuropsychological evaluation when the presentation is not typical and differentiation from pseudodementia secondary to depression is necessary. (**I**)

Key Point:

Early-stage HAD differs from Alzheimer's disease in that it is more likely to present with behavioral changes, progresses more rapidly, may be associated with abnormal cerebrospinal fluid (CSF) findings, and is rarely associated with aphasia.

Treatment

When patients receiving highly active antiretroviral therapy (HAART) present with symptoms of HAD, clinicians should assess the efficacy of the HAART regimen. (**III**)

When patients not receiving HAART present with symptoms of HAD, clinicians should initiate HAART (**III**)

HIV-Associated Myelopathy

Key Point:

HIV-associated myelopathy should be part of the differential diagnosis in men with erectile dysfunction, especially in the setting of normal testosterone levels.

Diagnosis

In the differential diagnosis for HIV-associated myelopathy, clinicians should exclude other treatable conditions that could cause spinal cord disease, particularly compressive lesions and other infectious or neoplastic etiologies. (**I**)

Clinicians should obtain the following blood tests in patients with suspected HIV-associated myelopathy: (**I**)

- Serum RPR or VDRL
- Toxoplasma antibodies
- Cryptococcal antigen
- Vitamin B_{12} level
- Human T-lymphocyte virus (HTLV) I/II antibodies

Clinicians should obtain neuroimaging studies of the spinal cord in all patients who present with suspected spinal cord disease. (**I**)

Treatment

Clinicians should prescribe symptomatic therapy to patients with HIV-associated myelopathy. (**I**)

Key Point:

The effect of HAART on improving the symptoms or slowing the progression of HIV-associated myelopathy is not known.

Peripheral Neuropathy

Distal Symmetric Polyneuropathy (DSP)

Diagnosis

Clinicians should obtain blood tests to screen for diabetes and vitamin B_{12} deficiency in the evaluation of a patient with suspected distal symmetric polyneuropathy. (**III**)

Clinicians should refer patients with more complex suspected or proven peripheral neuropathy syndromes to a neurologist to assist with the diagnosis and management. (**III**)

Key Point:

Electrophysiologic studies are of great value in diagnosing more complex non-DSP neuropathy in HIV-infected patients.

Treatment and Management

Clinicians should provide pain control for distal symmetric polyneuropathy, (**I**) which is achieved by a careful, systematic, and stepwise evaluation of the patient's response to available analgesic agents (see Figure 2 in the original guideline document).

Clinicians should initiate mild analgesics, including acetaminophen, aspirin, or other non-steroidal anti-inflammatory agents, with or without adjunctive agents (e.g., anticonvulsants, antidepressants, topical agents), as the first line of therapy for pain control. (**I**)

Clinicians should use narcotic analgesia when pain control is not achieved by first line and adjunctive measures. (**I**)

Clinicians should refer patients to a pain management specialist when adequate pain control cannot be achieved. (**I**)

In cases of ARV therapy-associated DSP, the decision to discontinue a neurotoxic antiretroviral (ARV) drug is not automatic and should only be made after carefully weighing the risks and benefits of virologic control versus neuropathic symptom control. (**III**)

Inflammatory Demyelinating Polyneuropathy (IDP)

Diagnosis

Clinicians should perform lumbar puncture and electromyography/nerve conduction velocities (EMG/NCV) in patients with suspected IDP. (**III**)

Key Point:

Inflammatory demyelinating polyneuropathy should be part of the differential diagnosis in HIV-infected patients presenting with progressive muscle weakness.

Treatment

Clinicians should initiate immunomodulating therapy, such as corticosteroids, high-dose intravenous immunoglobulin (2.0 gm/kg divided over 2 to 5 days), or plasmapheresis (4-5 exchanges), for patients with HIV-associated IDP. (**I**)

When IDP is associated with symptomatic hyperlactatemia or lactic acidosis, clinicians should immediately discontinue ARV therapy, especially nucleoside reverse transcriptase inhibitors (NRTIs). (**I**)

Mononeuropathy Multiplex (MM)

Diagnosis

Clinicians should establish the diagnosis and etiology of mononeuritis multiplex based on neurologic consultation, electrophysiologic studies, and/or nerve biopsy. (**III**)

Key Point:

Mononeuritis multiplex should be part of the differential diagnosis in HIV-infected patients presenting with asymmetric multifocal motor and sensory nerve abnormalities. Other etiologies, such as hepatitis B, may cause vasculitic mononeuropathy multiplex and should also be considered in the differential diagnosis.

Treatment

Clinicians should observe patients with early-onset MM because it may spontaneously resolve within weeks to several months. (**III**)

Clinicians should initiate HAART in patients with late-onset MM occurring in advanced HIV infection. (**I**)

Key Point:

Empiric therapy for cytomegalovirus (CMV) should be considered for patients with late-onset MM, particularly if CSF or nerve biopsy is revealing of CMV infection. However, there is no sufficient data to make any conclusive recommendation.

Progressive Polyradiculopathy (PP)

Diagnosis

Clinicians should establish the diagnosis of progressive polyradiculopathy based on neurologic consultation, spinal MRI, CSF analysis, and electrophysiologic studies. (**III**)

Key Point:

The severe and widespread proximal axonal pathology in lumbar nerve root segments help differentiate progressive polyradiculopathy from mononeuropathy multiplex or inflammatory demyelinating polyneuropathy.

Treatment

Clinicians should promptly initiate anti-CMV therapy for improvement of symptoms and/or stabilization of signs in progressive polyradiculopathy secondary to CMV. (**II**)

Clinicians should initiate or optimize HAART in patients with progressive polyradiculopathy. (**I**)

Myopathy

Diagnosis

Clinicians should use creatine phosphokinase (CPK) determinations combined with EMG and/or muscle biopsy to confirm the diagnosis of HIV-associated myopathy. (**III**)

Clinicians should consider referring patients to a neurologist or rheumatologist to confirm and manage HIV-associated myopathy. (**III**)

Key Point:

An isolated CPK elevation is not sufficient to make a diagnosis of myopathy without accompanying clinical features because CPK levels may be elevated from other causes.

HIV-Associated Neuromuscular Weakness Syndrome (HANWS)

Diagnosis

Clinicians should exclude other possible causes of weakness by performing a complete neurologic examination and obtaining blood tests. (**III**)

Clinicians should consult with a neurologist for evaluation and management of patients with suspected HANWS. (**III**)

Treatment

Clinicians should discontinue the use of NRTIs in patients with HANWS. (**I**)

For patients with HANWS, clinicians should initiate systemic treatment for lactic acidosis syndrome and supportive treatment for the neurologic component in a monitored setting. (**I**)

Definitions:

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for Management of Peripheral Neuropathy in an HIV-Infected Individual.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of human immunodeficiency virus (HIV)-associated neurologic complications

POTENTIAL HARMS

Adverse Effects of Medications

- *Corticosteroids* should be used with caution because of their immunosuppressant effects
- *Mexiletine* was associated with a high frequency of dose limiting side effects
- Adverse effects associated with *highly active antiretroviral therapy (HAART)*

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with HIV infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative, the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the NYSDOH Distribution Center for providers who lack internet access.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the Clinical Education Initiative (CEI) and the AIDS Education and Training Centers (AETC). The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Neurologic complications. New York (NY): New York State Department of Health; 2004 Mar. 26 p. [31 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Mar

GUIDELINE DEVELOPER(S)

New York State Department of Health - State/Local Government Agency [U.S.]

SOURCE(S) OF FUNDING

New York State Department of Health

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on September 10, 2007.

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Readers with questions regarding guideline content are directed to contact the guideline developer.

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